Claims

1. A MRI detectable species according to formula (I) which are incorporated into or onto the cells surface and characterised for a contrast sufficient to clearly distinguish between normal, healthy cells and tumor cells, wherein;

$$D_p\text{-}S_n\text{-}N_m \qquad (I)$$

D is a MRI detectable moiety selected from the group consisting of coated ferromagnetic particles, coated superparamagnetic particles and chelated complexes of paramagnetic metal ions;

S is a spacer;

N is a molecule of a nutrient or pseudo-nutrient comprising monosaccharides, essential amino acids and their derivatives, polyamines and non-essential amino-acids and n is an integer of 0 to 5, m is an integer of 1 to 5 and p is an integer of 1 to 10.

2. The MRI detectable species of claim 1 wherein D contains at least one site for a possible link to the spacer S or the nutrient/pseudo-nutrient molecule N.
3. The MRI detectable species of claim 1 and 2, wherein the moiety D is a chelated complex of a paramagnetic metal ion selected from the ions of transition and lanthanide metals with a chelating ligand L.
4. The MRI detectable species of claim 3, wherein the paramagnetic metal ion is selected from the ions having atomic number of 21 to 29, 42, 43, 44, or 57 to 71, and the chelating ligand L is selected from the group consisting of the residue of a polyaminopolycarboxylic acid, either linear or cyclic, in racemic or optically active form, such as ethylenediaminotetracetic acid (EDTA), diethylenetriaminopentaacetic acid (DTPA), N-[2-[bis(carboxymethyl) -amino]-3-(4-ethoxyphenyl)propyl]-N-[2-[bis(carboxymethyl)amino]ethyl]-L-glycine (EOB-DTPA), N,N-bis[2-[bis(carboxymethyl)amino]ethyl]-L-glutamic acid (DTPA-GLU), N,N-Bis[2-[bis(carboxymethyl)amino]ethyl]-L-γ-glutamyl-L-glutamine, N,N-bis[2-[bis(carboxymethyl)amino]ethyl]-L-lysine (DTPA-LYS), the DTPA mono- or bis-amide derivatives, such as N,N-bis[2-[carboxymethyl[(methylcarbamoyl) -methyl]amino]ethyl] glycine (DTPA-BMA), 4-carboxy-5,8,11-tris(carboxymethyl)-1-phenyl-2-oxa-5,8,11-triazatridecan-13-oic acid (BOPTA), 1,4,7,10-tetraazacyclo-dodecan-1,4,7,10-tetraacetic acid (DOTA),

1,4,7,10-tetraazacyclododecan-1,4,7-triacetic acid (DO3A), 10-(2-hydroxypropyl)-1,4,7,10-tetraazacyclododecan-1,4,7-triacetic acid (HPDO3A), 2-methyl-1,4,7,10-tetraazacyclododecan-1,4,7,10-tetraacetic acid (MCTA), (α,α',α",α"')-tetramethyl-1,4,7,10-tetraazacyclododecan-1,4,7,10-tetraacetic acid (DOTMA), 3,6,9,15-tetraazabicyclo[9.3.1]pentadeca-1(15),11,13-triene-3,6,9-triacetic acid (PCTA), [4-(1,6,10-triazaundecan)-phenyl-aminocarbonylmethyl]-1,4,7,10-tetraazacyclododecan-4,7,10-triacetic acid; a derivative thereof wherein one or more of the carboxylic groups are in the form of the corresponding salts, esters, or amides; and the residue of a corresponding compound wherein one or more of the carboxylic groups is replaced by a phosphonic and/or phosphinic group, such as for instance 4-carboxy-5,11-bis(carboxy -methyl)-1-phenyl-12-[(phenylmethoxy)methyl]-8-(phosphonomethyl)-2-oxa-5,8,11-triazatridecan-13-oic acid, N,N'-[(phosphonomethylimino)di-2,1-ethanediyl]bis[N-(carboxymethyl)glycine], N,N'-[(phosphonomethylimino)di-2,1-ethanediyl]bis[N-(phosphonomethyl)glycine], N,N'-[(phosphinomethylimino)di-2,1-ethanediyl]bis[N-(carboxymethyl)glycine], 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetrakis[methylen(methylphosphonic)]acid, or 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetrakis[methylen(methylphosphinic)]acid.

5. The MRI detectable species of formula (I) according to claims 1 to 4 wherein the complexes are formed with Mn, Fe, Eu, Gd or Dy ions.
6. The MRI detectable species of formula (I) according to any of the preceding claims 1 to 5 wherein the nutrient or pseudo-nutrient molecule N is selected from glucose, alanine, phenylalanine, lysine, arginine, putrescine, spermidine, spermine, asparagine, agmatine and glutamine.
7. The MRI detectable species of formula (I) according to any of the preceding claims 1 to 6, wherein the spacer S, if present, is a homo- or hetero-bifunctional linker where the two reactive moieties are separated by alkylidene, alkenylidene, alkynylidene, cycloalkylidene, arylidene, or aralkylidene radical that can be substituted and be interrupted by heteroatoms such as oxygen, nitrogen, and sulphur.
8. The MRI detectable species of formula (I) according to claim 7, wherein the reactive moieties are separated by an aliphatic, straight or branched chain, that may

be interrupted by –O-, -S-, -CO-, -NR-, -CS- and the like groups or by aromatic rings, and may be an –OR, -SR, -NRR_1, -COOR, -$CONRR_1$, and the like substituents, wherein R and R_1, each independently, may be a hydrogen atom or an organic group.

9. A process for the preparation of a MRI detectable species of formula (I) according to any of claims 1 to 8, said process comprising either

- conjugating the spacer S, if any, with the nutrient or pseudo-nutrient molecule N, and the thus obtained intermediate with the MRI detectable moiety D or a precursor thereof; or
- conjugating the MRI detectable moiety D or a precursor thereof with the spacer S, if any, and the thus obtained intermediate with the nutrient or pseuso-nutrient molecule N; and

when a precursor of the MRI detectable moiety D is used, converting said precursor into the desired MRI detectable moiety.

10. The process of claim 9 for the preparation of a MRI detectable species of claim 3, wherein a chelating ligand L is employed as precursor of the MRI detectable moiety D to afford an intermediate compound of formula (II)

$$L_p\text{-}S_n\text{-}N_m \qquad (II)$$

wherein L is a chelating ligand
S is a spacer
N is a molecule of a nutrient or pseudo-nutrient
n is 0 or an integer
m is an integer and
p is an integer,

wherein L, S, P, p, n and m are as defined above

and is converted into the desired end compound of formula (I) by metallation with a suitably selected paramagnetic metal ion.

11. An intermediate compound of formula (II)

$$L_p\text{-}S_n\text{-}N_m \qquad (II)$$

wherein L is a chelating ligand
S is a spacer
N is a molecule of a nutrient or pseudo-nutrient

n is 0 or an integer

m is an integer and

p is an integer

and wherein L, S, P, p, n and m are as defined above.

12. A compound according to Claim 11 selected from the following:

6,16-dicarbonyl-5,8,11,14,17-pentaaza-8,11,14-tricarboxymethyl-heneicosandiguadinine;

6,16-dicarbonyl-5,19-dicarboxy-5,8,11,14,17-pentaaza-8,11,14-tricarboxymethyl-heneicosandioic acid diamide;

3,6,9-triaza-3,6,9-tricarboxymethylundecanoic acid bis-glucopyranosylamide;

2,24-diamino-8,18-dicarbonyl-7,10,13,16,19-pentaaza-10,13,16-tricarboxymethyl-pentaheicosandioic acid;

2,16-dibenzyl-4,13-dicarbonyl-3,6,9,12,15-pentaaza-6,9,12-tricarboxymethyl-heptadecandioic acid;

10,20-dicarbonyl-4,9,12,15,18,21,26-heptaaza-12,15,18-tricarboxymethyl-nonaheicosan-1,29-diamine;

4,26-diamino-5,10,20,25-tetracarbonyl-12,15,18-tricarboxymethyl-6,9,12,15,18,21,24-heptaaza-nonaheicosan-1,29-diguanidina;

N,N-Bis[2-[bis(carboxymethyl)amino]ethyl]-L-γ-glutamyl-L-glutamine;

N,N-Bis[2-[bis(carboxymethyl)amino]ethyl]-L-γ-glutamyl-agmatine;

N,N-Bis[2-[bis(carboxymethyl)amino]ethyl]-L-γ-glutamyl-arginine;

[4-(1,6,10-triazaundecan)-phenyl-aminocarbonylmetl]-1,4,7,10-tetraazacyclododecan-4,7,10-triacetic acid

13. A pharmaceutical composition comprising an amount sufficient to give the desired contrast of a MRI detectable species of any of preceding claims 1 to 12 together with at least one pharmaceutically acceptable carrier.

14. A pharmaceutical composition according to claims 13 to obtain images of organs and/or tissues of human and animal body, through the use of nuclear magnetic resonance.

15. The pharmaceutical composition of claims 13 to 14 in the form of a pharmaceutically injectable composition.

16. The injectable composition of claim 15 for the diagnosis of tumors by MRI.